1152-131 Epicardial Fat as a Source of Inflammatory Burden

Tomasz Mazurek, LiFeng Zhang, John Mannion, Yuchuan Liu, Jack L. Martin, Arthur Martella, Yi Shi, Andrew Zalewski, Thomas Jefferson University, Philadelphia, PA

Background: Inflammatory mediators adversely influence coronary lesion formation. Although omental adipose tissue contributes to the inflammatory burden in patients with insulin resistance, the importance of other fat depots has not been elucidated. Accordingly, we examined properties of epicardial adipose tissue in patients undergoing CABG surgery.

Methods: Paired samples of epicardial (epi-fat) and subcutaneous (sc-fat) adipose tissue were harvested during elective CABG surgery (n=42; age: 65±10). Tissue expression of chemokine (MCP-1) and inflammatory cytokines (IL-6, IL-1β, TNF-α) was analyzed by real-time RT-PCR (mRNA), and ELISA (protein release over 3 hours).

Results: Higher expression of MCP-1, IL-6, IL-1β and TNF-α was observed in epi-fat, as compared with sc-fat (Table). These changes were evident on mRNA (target mRNA/GAPDH) and protein levels. Proinflammatory properties of epi-fat were noted in diabetics (n=25) and non-diabetics (n=17) or in those with BMI ≥30 kg/m^2 (n=22) and <30 kg/m^2 (n=20) (NS between the groups). The use of statins (n=20) or ACE inhibitors (n=15) prior to CABG was insufficient to attenuate epicardial inflammatory reaction.

Conclusions: 1. Epicardial (pericoronary) adipose tissue may contribute to a low-grade inflammation in high risk cardiac patients; 2. Coronary arteries are exposed to inflammatory signals from the perivascular tissue; 3. Current therapies fail to attenuate local inflammatory burden.

Tissues n=42	MCP-1		IL-6		IL-1β		TNF-α	
	mRNA	Protein (ng/g)	mRNA	Protein (ng/g)	mRNA	Protein (pg/g)	mRNA	Protein (pg/g)
Epi-fat	6.2±1.3	53.9±6.7	6.4±1.8	57.3±6.1	13.9±3.6	28.7±6.6	1.3±0.4	54.2±9.0
Sc-fat	2.0±0.3	26.4±4.0	1.0±0.3	21.6±4.0	5.1±0.1	8.0±2.6	0.4±0.1	15.2±3.6
	p<0.001	p<0.001	p<0.01	p<0.001	p<0.05	p<0.01	p<0.05	p<0.001

1152-132 Rosuvastatin Improves Endothelial Cell Function in Glutathione Peroxidase Deficient Mice

John Jones, Joseph Loscalzo, Boston University Medical Center, Boston, MA

Background: HMG-CoA reductase inhibitors (statins) have been shown to possess vasculoprotective activity independent of their lipid-lowering properties. Previous studies have shown that mice with homozygous deficiency in cellular glutathione peroxidase (GPx-1(-/-)) have impaired endothelial function owing to an increase in vascular oxidant stress. In this study, we investigated whether rosuvastatin can improve the endothelial dysfunction of GPx-1(-/-) mice.

Methods: Mice were divided into 4 groups: wild-type + rosuvastatin (RSV), wild-type + vehicle, GPx-1(-/-) + RSV, and GPx-1(-/-) + vehicle. Mice were treated with daily subcutaneous injections of either RSV (10 mg/kg/day) or vehicle for 1 week. Videomicroscopy was then used to assess the reactivity of the mesenteric arterioles (20-50 microns in diameter) in response to superfusion with methacholine (100 nM – 100 μM).

Results: The GPx-1(-/-) + vehicle group demonstrated paradoxical vasoconstriction in response to methacholine compared to the wild-type + vehicle group (+2.9 ± -1.3% change vs. −5.3 ± -2.9% change, respectively; p<0.05). Treatment with RSV partially corrected the endothelial dysfunction of the GPx-1(-/-) mice (-2.6 ± -1.0% change vs. +2.9 ± -1.3% change for GPx-1(-/-) + RSV and GPx-1(-/-) + vehicle, respectively; p<0.05).

Conclusion: This study demonstrates that rosuvastatin can improve endothelial function in GPx-1(-/-) mice. In that the GPx-1(-/-) mouse is a model of oxidant stress in the absence of hypercholesterolemia, these data support the view that rosuvastatin can improve endothelial function by an antioxidant mechanism.

POSTER SESSION

1153 Arterial Biomechanics

Tuesday, April 01, 2003, 9:00 a.m.-11:00 a.m.
McCormick Place, Hall A
Presentation Hour: 10:00 a.m.-11:00 a.m.

1153-134 Identifying Early Changes in Children at Risk for Cardiovascular Disease: Echo-Doppler Assessment of the Biophysical Properties of the Aorta in Children Born Small for Gestational Age

Timothy J. Bradley, James E. Potts, Mary T. Potts, Astrid De Souza, Shoo K. Lee, George G. Sandor, Children's and Women's Health Centre of B.C., Vancouver, BC, Canada

Background: Low birth weight and the intrauterine growth environment have been shown to be associated with adult cardiovascular risk. We used an Echo-Doppler method to assess the biophysical properties of the aorta in children born small for gestational age (SGA) and determine associations with known perinatal risk factors.

Methods: Thirty-nine SGA and 41 controls aged 8 to 13 years were studied. Perinatal risk factors (gestational age, birth weight, mother's age, birth rank order, maternal hypertension in pregnancy, smoking exposure, breast feeding and significant family history) were recorded. The aortic diameters and pulse wave transit time around the aortic arch were measured using Echo-Doppler and the blood pressure recorded. The pulse wave velocity (PWV), aortic input impedance (Zi), characteristic impedance (Zc), arterial pressure-strain elastic modulus (Ep), and arterial wall stiffness index (β_{index}) were calculated. Differences were determined using analysis of variance and relationships were tested using linear or logistic regression.

Results: Birth weight and gestational age were lower in SGA (1977 ± 550 vs 3441 ± 571 g, 37 ± 3 vs 39 ± 3 weeks). SGA remained smaller (BMI 16.8 ± 2.5 vs 19.3 ± 3.9 kg/m^2, p<0.001), with smaller aortic diameters (aortic annulus 1.66 ± 0.12 vs 1.79 ± 0.17 cm, p<0.0004; ascending aorta in systole 2.01 ± 0.23 vs 2.22 ± 0.24 cm, p<0.0001; ascending aorta in diastole, 1.74 ± 0.22 vs 1.87 ± 0.21 cm, p<0.001). SGA had lower systolic and diastolic blood pressures (102 ± 9 vs 108 ± 9 mmHg, p< 0.02 and 61 ± 9 vs 68 ± 9 mmHg, p< 0.008), but pulse pressure was similar. The vascular indices were all higher in SGA (PWV 374 ± 46 vs 348 ± 47 cm/s, p< 0.02; Zi 177 ± 39 vs 142 ± 27 dynes•s/cm^5, p< 0.0001; Zc 185 ± 29 vs 152 ± 37 dynes•s/cm^5, p< 0.0001; Ep 286 ± 101 vs 216 ± 41mmHg, p< 0.0001; and β_{index} 2.43 ± 0.32 vs 2.17 ± 0.15, p< 0.0001). There were negative associations between: birth weight and Zi, Zc, Ep, β_{index}; and BMI and Zi, Zc. In this cohort, no association was found between birth weight and blood pressure.

Conclusions: Abnormal vascular impedance and stiffness indices can be detected in SGA using Echo-Doppler. Low birth weight is associated with abnormal biophysical properties of the aorta in childhood.

1153-135 Elevated Brain Natriuretic Peptide Levels Are Related to Impaired Small Artery Elasticity

Venkatakrishna N. Tholakanahalli, Daniel Duprez, Lynn Hoke, Jay Cohn, University of Minnesota, Minneapolis, MN

Background: Brain Natriuretic Peptide (BNP) is an important serum marker in detecting ventricular dysfunction. Although its role in asymptomatic individuals has been correlated with subclinical cardiovascular disease, its significance, as a marker of vascular disease is largely unknown. The objective of this study is to determine if there is a relationship between elevated BNP levels and arterial stiffness in asymptomatic subjects, and hence it's role in vascular disease.

Methods: Asymptomatic individuals with elevated BNP, who attended cardiovascular primary prevention center, were divided into two age-matched groups: one group, with borderline BNP (50-99 pg/ml) and other group with elevated BNP (>100pg/ml). Large (C1) and small (C2) arterial elasticity indices were derived from radial pulse contour analysis using the modified Windkessel model. The relationship between borderline BNP, elevated BNP, combined borderline and elevated groups with C1 and C2 were derived using spearman rank correlation coefficient.

Results: In borderline group (n=23) the mean BNP level was 68.1, ranging from 51-90 while in elevated group (n=13) the mean BNP level was 154.9 ranging from 111 to 293. In elevated BNP group, C2 (mean 4.14± 0.78 SE, ml/mmHg x 100) correlated significantly with BNP (p<0.01). C2 was also strongly associated with elevated BNP group in comparison with borderline BNP group (p<0.03). Neither C1 in the elevated BNP group (P=0.1) nor C1 in borderline BNP group (p=0.9) were related to BNP.

Conclusions: BNP can be considered as a useful serum marker of changes in small artery elasticity enabling the detection of early vascular disease and in turn possibly endothelial dysfunction.

1153-136 Culprit Coronary Lesion Location Correlates Closely With Aortic Root Mechanics Early After Acute Myocardial Infarction

Spyros G. Lambrou, Constantina Aggeli, Dimosthenis Panagiotakos, Christos Pitsavos, Christodoulos Stefanadis, Pavlos Toutouzas, University of Athens, Athens, Greece

The aortic (ao) root is nourished by vasa vasorum (vv) originating from the coronary arteries (CA). Experimental vv flow disruption induces medial ischemia and deteriorates ao root elasticity. Whether similar effects occur in cases of spontaneous CA occlusion is unknown.

Methods: Transthoracic echo and CA angiogram were performed consecutively in 76 hospitalized pts (aged 56+-11 yrs, 64 male) with a first MI. Ao root diameters were measured by 2D-guided M-mode echo; Blood pressure (BP) was measured by arm sphygmomanometry. Two indices of ao root mechanics were calculated blindly: 1) Distensibility (D)=2 x (pulsatile change in ao diameter) / ([diastolic ao diameter] x [pulse pressure]); 2) Stiffness index β=[ln (systolic pressure)/(diastolic pressure)] x diastolic diameter / pulsatile change in diameter. Carotid-femoral pulse wave velocity (PWV) was measured as an index of overall ao stiffness. Considering the origin of the ao root vv (predominantly: central parts of the left CA), pts were grouped by culprit lesion location in group A: lesion in proximal LAD, middle LAD or proximal LCx (n=35), and group B: lesion in distal LAD, distal LCx or entire RCA (n=33).

Results: Pts in group A were older (60+-10 vs 53+-12 yrs, p=0.01); The groups did not differ in ao dimensions, BP, CAD extent, culprit CA patency, or drug treatment. Significant unidirectional (stiffer ao root in group A) differences were found between groups regarding indices of ao root elasticity (A vs B; D: 1.1+-0.7 vs 1.8+-0.8 dynes-1.cm2.10-6; β: 19.3+-10.9 vs 10.4+-5.0, both p<0.001). PWV did not differ between groups (A vs B: 10.2+-2.9 vs 9.9+-3.9 m/s, p=NS). Lesion location (as A vs B) was a significant predictor of both D and β (b=0.08, p=0.007; b=-0.113, p=0.006), independently of age and BP. Conversely, lesion location did not predict PWV. Indices of ao root mechanics correlated poorly with PWV.

Conclusions: A significant association links culprit CA lesion location to early post-MI ao root mechanics. This is partly unaccounted for by pressure-dependent mechanisms, it is compatible with the anatomy of ao root vascularization and it implies that the ao root occasionally forms part of the territory afflicted by CA occlusion.